The Effects of Real-Time and Intermittently Scanned Continuous Glucose Monitoring on Glycemic Control in Veterans with Type Two Diabetes

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Abstract

Purpose:

Diabetes is more prevalent among US veterans than the general population. The Department of Veterans Affairs (VA) continuous glucose monitoring (CGM) updated guidance and the Veterans Integrated Services Network (VISN) 19 and 21 criteria for use includes veterans with type-two diabetes mellitus (T2DM) on multiple daily injections of insulin (≥3 injections/day) and significant hypoglycemia history. The available literature data have shown only modest reductions in HbA1c in patients with T2DM treated with CGM systems. This quality improvement project aims to analyze the change in glycemic control afforded by CGM systems in veterans with T2DM located in VISN 19 and 21.

Methods:

This retrospective multisite cohort project will evaluate veterans with T2DM not on an insulin pump with at least one fill for a real-time continuous glucose monitoring system (rtCGM) or an intermittently scanned continuous glucose monitoring system (isCGM) from July 14th, 2017, to December 1st, 2022. Pregnant veterans with gestational diabetes and veterans with type-one diabetes mellitus will be excluded. Baseline characteristics include demographics, relevant comorbidities, HbA1c, insulin type, number of insulin injections per day, CGM system, VA prescriptions for hypoglycemia mitigation agents, and diabetes related general inpatient admissions and emergency department (ED) visits six months pre-CGM implementation. The primary outcome is change in veterans HbA1c six months post-implementation of the CGM system compared to six months pre-implementation. Secondary outcomes include change in inpatient admissions and ED visits post-CGM implementation, and diabetes outpatient visits post-CGM initiation. Descriptive outcomes include a chart review of a random sample of veterans to determine if they are successfully reporting their data to their providers, CGM sensor adherence, and CGM discontinuation rates. All data will be collected from the VA Corporate Data Warehouse, a copy of VA's electronic health record. A multivariate model will be used to estimate the effect of CGM initiation on the HbA1c change from baseline at 6 months. Patients will serve as their own control. A similar analytic approach will be utilized for secondary outcomes.

Preliminary Results:

The preliminary analysis for the primary outcome included 1,954 veterans across 15 healthcare systems in VISN 19 and 21. Of these veterans, 1,468 had fills for an isCGM system and 486 had a fill for a rtCGM system. The average HbA1c in the overall patient population decreased from a baseline of 8.80% to 8.15% six months after the initial fill of a CGM system [difference -0.65%, 95% confidence interval (CI) -0.58 to -0.72]. The preliminary analysis did not account for any confounders and is only evaluating the average HbA1c at baseline and six months after the first fill of a CGM system.

Discussion:

In the preliminary analysis, CGM systems showed a statistically significant decrease in HbA1c from baseline six months after the first fill of a CGM system. It remains to be seen if these results will be maintained in the long-term.

Introduction:

The Department of Veterans Affairs (VA) continuous glucose monitoring (CGM) updated guidance[1] and the Veterans Integrated Services Network (VISN) 19 and VISN 21 criteria for use[2] (CFU) includes veterans with type 2 diabetes (T2DM) on multiple daily injections (MDI) of insulin (≥3 injections/day) and those with significant hypoglycemia history. The current available evidence shows only modest benefits of CGM in reducing the glycosylated hemoglobin A1c (HbA1c) in this patient population. The VA currently utilizes the following rtCGM systems that are stand-alone[2]: Dexcom G6 and the Medtronic Guardian MMT-7020. The VA also has available the following intermittent continuous glucose monitoring (isCGM) systems[2]: Freestyle Libre 14 Day and Freestyle Libre 2.

It is estimated that more than 50% of patients with T2DM treated with insulin have an HbA1c ≥ 8%.[3] Diabetes is more prevalent among US veterans than the general population, possibly attributable to a higher prevalence of obesity in this population.[4] The American Diabetes Association (ADA) recommends offering real-time Continuous Glucose Monitoring (rtCGM) for diabetes management in adults with diabetes on multiple daily injections (MDI) of subcutaneous insulin or on basal insulin who can use devices safely (Grade A).[5] The ADA further states isCGM can be used for diabetes management in adults with diabetes on MDI of subcutaneous insulin (Grade B) or basal insulin (Grade C).[5]

Randomized controlled trial (RCT) data have consistently shown reductions in A1c in patients with T2DM treated with rtCGM[6-9]. The DIAMOND Study (n=158) showed an adjusted difference in HbA1c of -0.3% [95% confidence interval (CI), -0.5% to 0.0%] with the rtCGM system Dexcom G4 at 24 weeks compared with self-monitoring of blood glucose (SMBG).[6] The MOBILE study group (n=175) found an adjusted difference in HbA1c of -0.4% [95%CI, −0.8% to −0.1%] with

the rtCGM system Dexcom G6 at 8 months compared with SMBG.[7] Yaron and colleagues (n=101) found a decrease in HbA1c of -0.85% from baseline at 10 weeks with the isCGM system FreeStyle Libre compared to a difference from baseline at 10 weeks of -0.32% with SMBG in the intention to treat analysis when adjusted for baseline HbA1c.[8] The Replace study (n=204) found no difference between intervention (FreeStyle Libre) and control (SMBG) in the change in HbA1c at 6 months.[9]

As the costs of diabetes care in the US continues to soar, it is imperative to find effective strategies to accomplish glycemic control.[10] The Quality Improvement (QI) project aims to analyze the glycemic control afforded by CGM systems in veterans with T2DM located in VISN 19 and VISN 21. This quality improvement project will evaluate if these glycemic benefits are translating to our veteran population on rtCGM, as well as ensuring that appropriate follow-up is occurring in our health system.

Methods:

This study has been approved by the University of Nevada, Reno Institutional Review Board (IRB) as not human subject research.

Study Population and Data Source:

All data will be collected from the VA Corporate Data Warehouse (CDW) via Structured Query Language (SQL) queries. Veterans with T2DM from sixteen medical centers in VISN 19 and VISN 21 with at least one fill for a rtCGM stand-alone system or isCGM system from July 14th, 2017, to February 1st, 2022, will be eligible for inclusion in the project. If a veteran had fill for multiple types of CGM systems, only the first CGM system filled would be included in the primary analysis.

Veterans with a diagnosis of type 1 diabetes mellitus (T1DM), paraneoplastic syndromes, CGM fill related to pregnancy or gastrectomy, and veterans on an insulin pump will be excluded. VISN 19 includes 8 healthcare systems and 123 additional sites of care covering the states of Utah, Montana, Wyoming, Colorado, Oklahoma and portions of Idaho, Kansas, Nebraska, Nevada and North Dakota. VISN 21 includes 7 healthcare systems and 67 additional sites of care in northern and central California, Nevada, Hawaii, the Philippines, and U.S. Territories in the Pacific Basin. If a veteran had a diagnosis for T1DM and T2DM, their prescription history was pulled to see if their medication profile gave indication to what the correct diagnosis was. Medications queried include those typically only used to treat T2DM: acarbose, dipeptidyl peptidase 4 inhibitors, glucagon like-peptide 1 agonists, meglitinides, metformin, sodium-glucose cotransporter-2 inhibitors, sulfonylureas, and thiazolidinediones.[11]

The baseline characteristics that will be collected include demographics, relevant comorbidities, HbA1c, insulin type, number of insulin injections per day, CGM system, VA prescriptions for

hypoglycemia mitigation agents, and diabetes related general inpatient admissions and emergency department (ED) visits six months pre-CGM implementation

Outcomes:

The primary outcome will evaluate veterans HbA1c 6-months pre-implementation of CGM and 6-months (± 2 months) post-implementation. If veterans do not have a recorded HbA1c on file for evaluation of the primary outcome, they will be excluded. Secondary outcomes include measuring the change in HbA1c at 12-months if available, change in inpatient admissions and ED visits post-CGM implementation, and diabetes outpatient visits post-CGM initiation. A chart review of 10% of the veterans included in the study will be undertaken to determine what percent are successfully reporting their CGM data to their providers Descriptive outcomes CGM sensor adherence, and CGM discontinuation rates.

Statistical Analysis:

Descriptive statistics will be used to analyze the baseline characteristics. A multivariate model will be used to estimate the effect of CGM initiation on the A1c change (paired t test) from baseline at 6 months while controlling for confounding by individual covariates. Patients will serve as their own control. Covariates of interest will include demographics, type of CGM, concomitant medications, baseline A1c, adherence, and diabetic comorbidities and evaluated in bivariate models (T-test will be utilized if the outcomes are continuous, and Chi-square will be utilized if variables are categorical/dichotomous) and included in the multivariate model through a stepwise iterative model building process. For secondary outcomes a similar analytic approach will be utilized for 6 months change in A1c. For dichotomous outcomes (e.g. yes/no hospital admission, ED visit) we will use logistic regression models to evaluate the effect of CGM initiation on the health utilization outcome with similar methods to consider confounding by covariates that may independently influence the outcome of interest.

Preliminary Results

Patient Population

There were 4,081 veterans with T2DM with at least one fill for a CGM system from 07/14/2017 to 02/01/2022 at the 15 healthcare systems located in VISN 19 and 21. Of these veterans, 1,954 were included for the primary analysis. The reasons for exclusion can be seen in figure 1. The average age of the population was 68 years old. One thousand and eighteen (93%) of the veterans were male. Nine hundred and eighty-one (50%) of the veterans had at least one fill for an anti-hypoglycemic agent.

The average HbA1c in the overall patient population decreased from a baseline of 8.80% to 8.15% six months after the initial fill of a CGM system [difference -0.65%, 95% confidence interval (CI) -0.58 to -0.72]. For veterans who filled an isCGM systems, the average HbA1c

decreased from a baseline of 8.95% to 8.25% six months after the initial fill of an isCGM system [difference -0.70%, 95% CI -0.62 to -0.79]. For veterans who filled a rtCGM systems, the average HbA1c decreased from a baseline of 8.34% to 7.85% six months after the initial fill of a rtCGM system [difference -0.48%, 95% CI -0.36 to -0.60]. These results are depicted in Table 1.

Figure 1. Patient Flow

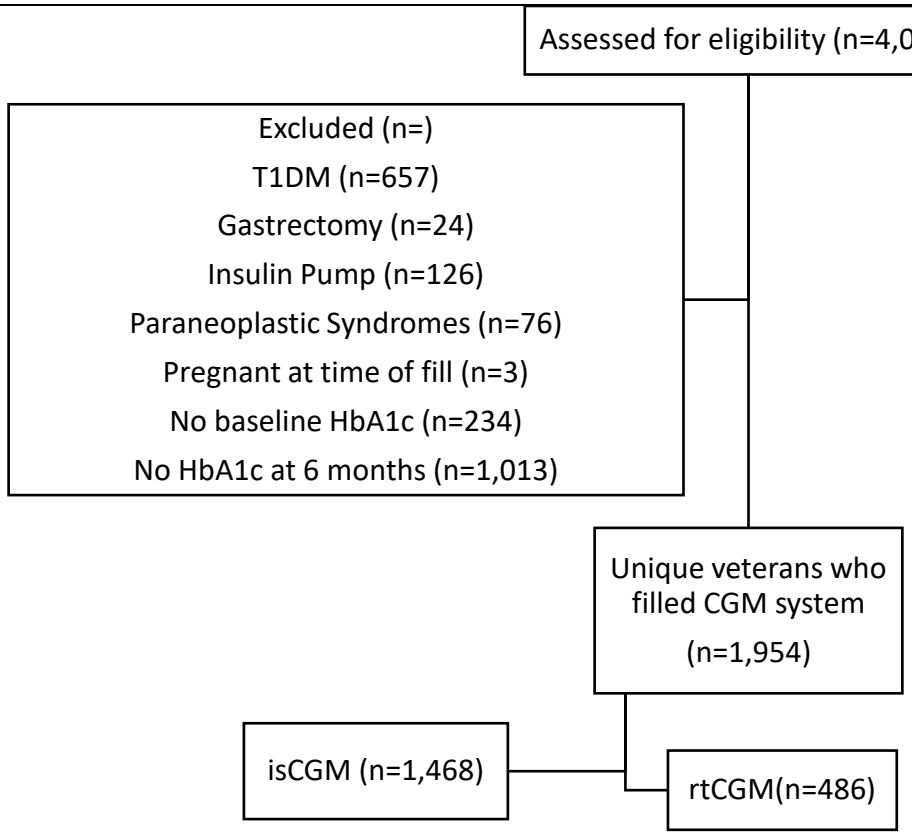

Table 1: Primary Outcome of HbA1c change 6 ± 2 Months Post First CGM Fill

CGM System	Pre-implementation	Post-implementation	Difference
isCGM (n=1,468)	8.95%	8.25%	-0.70% [95% CI-0.62 to -0.79, p < 0.001]
rtCGM (n=486)	8.34%	7.85%	-0.48% [95% CI -0.36 to -0.60 , p < 0.001]
Overall (n=1,954)	8.80%	8.15%	-0.65% [95% CI -0.58 to -0.72, p < 0.001]

Discussion

Preliminary results do not include any potential confounders and are only comparing average HbA1c values at baseline and at six months post-implementation of the veterans first fill for a CGM system. The preliminary results showcased a statistically significant decrease in HbA1c in the overall patient population. The preliminary results also showed a statistically significant decrease in HbA1c from baseline at six months with both the isCGM system and the rtCGM system.

Although there are stronger recommendations for the rtCGM systems in the ADA guidelines[5], there is a higher usage of isCGM systems in VISN 19 and 21, likely due to provider familiarity with the product. The veterans utilizing isCGM systems had a numerically higher baseline HbA1c than the rtCGM system veteran population.

A decrease in HbA1c from an intervention >0.5% is generally considered a clinically significant decrease in HbA1c, showcasing the utility the CGM systems can have in short-term HbA1c control.[12] The results showcased in this retrospective project appear at first glance to show stronger HbA1c control than what was seen in randomized controlled trials evaluating Dexcom G4, Dexcom G6, and the FreeStyle Libre.

CGM systems offer a wide variety of trackable metrics to evaluate glycemic control that were not able to be evaluated in this project due to access limitations. Trackable metrics include glycemic variability, time above range, time in range, time below range, and more. Some systems also provide alerts or alarms to help patients be aware of trends in their glycemic control.[5,13] It remains to be seen if these results will be translated into long-term control with regards to the HbA1c. Key secondary outcomes will evaluate the sustainability of these reductions at 9 and 12 months when that information is available in the CDW database. A chart review will also be performed on 10% of the population to see if veterans are appropriately sharing their CGM metrics with their providers.

Limitations of the project include not evaluating for any potential confounders, although that is planned by the project team as the next steps of the QI project. Veterans with fills for corticosteroids or other medications that can influence glycemic parameters were not excluded and could have negatively impacted the change in HbA1c change. There is also the potential for diagnostic coding errors that could lead to certain veterans being inappropriately excluded from the project, especially regarding T1DM. Although strategies outlined in the methods were utilized to minimize the number of veterans who would be inappropriately excluded, there were still 657 veterans who were excluded for having a diagnosis for T1DM and T2DM.

Disclosures:

The authors of this presentation have nothing to disclose concerning possible financial or personal relationships with commercial entities that may have a direct or indirect interest in the

subject matter of this presentation. This project has been approved as a quality improvement project. The project is supported by VA Pharmacy Residency Training and Education Program. The contents of this presentation/poster represent the views of the project manager and do not represent the views of the Department of Veterans Affairs or the United States Government.

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